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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/680,879	10/07/2003	Larry A. Wheeler	17529(AP)	9458

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ALLERGAN, INC.
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EXAMINER	
SOROUSH, LAYLA	

ART UNIT	PAPER NUMBER
1627	

NOTIFICATION DATE	DELIVERY MODE
05/05/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents_ip@allergan.com

Office Action Summary	**Application No.** 10/680,879	**Applicant(s)** WHEELER ET AL.	
	Examiner LAYLA SOROUSH	**Art Unit** 1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2011*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-13,21 and 23-25* is/are pending in the application.
  4a) Of the above claim(s) *21 and 23-25* is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *10-13* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
  Paper No(s)/Mail Date *11/22/10*.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 19, 2011 has been entered.

The original restriction election is carried over from the response to the office action mailed on December 28, 2006.

The following rejections are made:

Claim Objections

Claim 11 is objected to as being dependent upon a rejected base claim.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10, 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al. (WO 0236162 A2 –previously presented) in view of Hinton et al. (Optic-nerve degeneration in Alzheimer's disease, Volume 315:485-487, August 21, 1986, Number 8 –previously presented), Scahill et al. **(**A Placebo-Controlled Study of

Guanfacine in the Treatment of Children With Tic Disorders and Attention Deficit Hyperactivity Disorder Am J Psychiatry 158:1067-1074, July 2001) and Riekkinen Jr. et al. (THA Improves Word Priming and Clonidine Enhances Fluency and Working Memory in Alzheimer's Disease. Neuropsycho-pharmacology (1999) **20** 357-364).

Burke et al. teaches AGN 923 and chlonidine are neuroprotective agents (such as an alpha-adrenergic agonist) in an amount effective "to reduce the amount of cell death among the neurons of the retina and optic nerve (e.g. photoreceptors, retinal ganglion cells, and bipolar cell, or any of these) (p. 9-10)."

Burke et al. fails to specifically teach treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with the compound claimed.

Hinton et al. teaches "Alzheimer's disease is a dementing disorder of unknown cause in which there is degeneration of neuronal subpopulations in the central nervous system. In postmortem studies, we found widespread axonal degeneration in the optic nerves of 8 of 10 patients with Alzheimer's disease. The retinas of four of the patients were also examined histologically, and three had a reduction in the number of ganglion cells and in the thickness of the nerve-fiber layer. There was no retinal neurofibrillary degeneration or amyloid angiopathy, which are typically seen in the brains of patients with Alzheimer's disease. The changes we observed in the patients with Alzheimer's disease were clearly distinguishable from the findings in 10 age-matched controls and represent a sensory-system degeneration that occurs in Alzheimer's disease. Study of the retina in patients with this disease may be helpful diagnostically, and isolation of the affected ganglion cells may facilitate molecular analysis of the disorder."

Additionally, Scahill et al. teaches Clonidine also has a higher affinity than guanfacine for α_{2B}-receptors, which are prominent in the thalamus.

Riekkinen Jr. et al. is solely used to show the effects of an α 2-agonist, clonidine (0.5 and 2m g/kg, orally), on neuropsychologic performance in two groups of patients with Alzheimer's disease (AD). Clonidine enhanced a spatial working memory.

Therefore, one of ordinary skill in the art would have reasonable expectation of treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923. The motivation to treat a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923 is because (1) it is a neuroprotective agent (such as an alpha-adrenergic agonist) used "to reduce the amount of cell death among the neurons of the retina and optic nerve (e.g. photoreceptors, retinal ganglion cells, and bipolar cell, or any of these) (p. 9-10)" (2) Hinton et al. teaches the correlation between axonal degeneration in the optic nerves and patients with Alzheimer's disease and (3) the combination of Scahill et al. and Riekkinen Jr. et al. teaches Clonidine, an α 2-agonist, having higher affinity for α_{2B}-receptors, is useful for treating spatial working memory in patients with Alzheimer's disease. Hence, a skilled artisan would have reasonable expectation of successfully treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923.

Claims 10, 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burke et al. (US 2002/0094998 A1–previously presented) in view of Hinton et al.

(Optic-nerve degeneration in Alzheimer's disease, Volume 315:485-487, August 21, 1986, Number 8 –previously presented), Scahill et al. **(**A Placebo-Controlled Study of Guanfacine in the Treatment of Children With Tic Disorders and Attention Deficit Hyperactivity Disorder Am J Psychiatry 158:1067-1074, July 2001) and Riekkinen Jr. et al. (THA Improves Word Priming and Clonidine Enhances Fluency and Working Memory in Alzheimer's Disease. Neuropsycho-pharmacology (1999) 20 357-364).

Burke et al. teaches AGN 923 is a neuroprotective agent (such as an alpha-adrenergic agonist) in an amount effective "to reduce the amount of cell death among the neurons of the retina and optic nerve (e.g. photoreceptors, retinal ganglion cells, and bipolar cell, or any of these) [0026-7]."

Burke et al. fails to specifically teach treatment of Alzheimer's disease with the compound claimed.

Hinton et al. teaches "Alzheimer's disease is a dementing disorder of unknown cause in which there is degeneration of neuronal subpopulations in the central nervous system. In postmortem studies, we found widespread axonal degeneration in the optic nerves of 8 of 10 patients with Alzheimer's disease. The retinas of four of the patients were also examined histologically, and three had a reduction in the number of ganglion cells and in the thickness of the nerve-fiber layer. There was no retinal neurofibrillary degeneration or amyloid angiopathy, which are typically seen in the brains of patients with Alzheimer's disease. The changes we observed in the patients with Alzheimer's disease were clearly distinguishable from the findings in 10 age-matched controls and represent a sensory-system degeneration that occurs in Alzheimer's disease. Study of the retina in patients with this disease may be helpful diagnostically, and isolation of the affected ganglion cells may facilitate molecular analysis of the disorder."

Therefore, one of ordinary skill in the art would have reasonable expectation of treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923. The motivation to treat a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923 is because (1) it is a neuroprotective agent (such as an alpha-adrenergic agonist) used "to reduce the amount of cell death among the neurons of the retina and optic nerve (e.g. photoreceptors, retinal ganglion cells, and bipolar cell, or any of these) (p. 9-10)" (2) Hinton et al. teaches the correlation between axonal degeneration in the optic nerves and patients with Alzheimer's disease and (3) the combination of Scahill et al. and Riekkinen Jr. et al. teaches Clonidine, an α 2-agonist, having higher affinity for α_{2B}-receptors, is useful for treating spatial working memory in patients with Alzheimer's disease. Hence, a skilled artisan would have reasonable expectation of successfully treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Omum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (c)or 1.321 (d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3173(b).

Claims 10-11 and 13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 43, 49, and 71-72 of copending Application No. 10/881,761. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method for treating a neurodegenerative condition of the brain comprising administering an effective amount of a selective alpha 2B or selective 2B/2C adrenergic receptor agonist. The claims of Application No. 10/881,761 are likewise drawn to a method for treating neurodegenerative conditions of the brain comprising administration of an effective amount of a selective alpha 2B or alpha 2B/2C adrenergic receptor agonist. Both Applications are drawn to a method of treating neurodegenerative conditions by administering an alpha 2 receptor agonist; therefore, it would be obvious to use the alpha 2 receptor agonist AGN 197075 from the claimed invention as the alpha 2B or alpha 2B/2C adrenergic receptor agonist of Application No. 10/881,761.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented

Response to Arguments

Applicant's arguments that “What has not been known - and what the Burke reference does not suggest or disclose - is that there are alpha-2B or 2C receptors in those areas of the brain responsible for Alzheimer's disease in any non-trivial amount: not been thought that such agents would be effective agents for the treatment of neurodegenerative conditions of the brain, such as Alzheimer's disease and Parkinson's disease, since it has previously not been thought that alpha 2B and/or alpha 2C receptors were plentiful in these areas of the brain.” The Examiner states that the combination of Scahill et al. and Riekkinen Jr. et al. teaches Clonidine, an α 2-agonist, having higher affinity for α_{2B}-receptors, is useful for treating spatial working memory in patients with Alzheimer’s disease.

Additionally, Applicant's argument that the administration of α adrenergic receptor agonists are associated with major side effects of sedating the patient and therefore, there is no motivation to treat Alzheimer's disease with said compound is not persuasive. Examiner respectfully points out it is clear that the side effects do not occur over the entire treated population and as with any drug, a small population of patients experience such side effects. A skilled artisan would not deter from practicing the use of treating Alzheimer's disease with the said α adrenergic receptor agonists, as obviated by the prior art teachings.

Applicant argues a compound that is neuroprotective in the eye (or protecting the optic nerve) does not necessarily mean that it will be neuroprotective in the brain. In response, the Court has held that "the test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965). "There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdiqital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997). An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 82 USPQ2d 1385 (U.S. 2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results."). In this case, one of ordinary skill in the art would have reasonable expectation of treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923. The motivation to treat a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923 is because (1) it is a neuroprotective agent (such as an alpha-adrenergic agonist) used "to reduce the amount of cell death among the neurons of the retina and optic nerve (e.g. photoreceptors, retinal ganglion cells, and bipolar cell, or any of these) (p. 9-10)" (2) Hinton et al. teaches the correlation between axonal degeneration in the optic nerves and patients with Alzheimer's disease and (3) the combination of Scahill et al. and Riekkinen Jr. et al. teaches Clonidine, an α 2-

agonist, having higher affinity for α_{2B}-receptors, is useful for treating spatial working memory in patients with Alzheimer's disease. Hence, a skilled artisan would have reasonable expectation of successfully treating a mammal experiencing death or degeneration of neural cells related to Alzheimer's disease with AGN 923.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Layla Soroush whose telephone number is (571)272-5008. The examiner can normally be reached on Monday through Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627